REMARKS

Claims 11, 12, 14-18, 20-21 and 26-27 are pending in the application. Claims 11, 14 and 21 are amended herein. Claims 1-10, 13, 19, and 22-25 are cancelled. Claim 11 has been amended to incorporate the subject matter of claim 13 and further define the diffusion agent as being water in an amount of between 1 and 50% by weight with respect to the total weight (support for this amendment may be found at least in cancelled claim 19 and the cancelled subject matter of claim 21). Claims 14 and 21 have been amended to correct the dependency and claim scope in view of the amendments to claim 11. Claim 27 is newly added. Support for new claim 27 may be found at least in paragraph [0052] of the specification. Entry and consideration of the amendments and new claims are respectfully requested.

Rejections under 35 U.S.C.§103

Claims 11-13, 15-21 and 26 have rejected under 35 U.S.C. 103(a) as being obvious over Junco et al. (Journal of Inclusion Phenomena and Macrocyclic Chemistry, 2002, 44, 69-73, of record) in view of Majid et al. (US Patent 5,070,081, issued 3 Dec 1991, cited in PTO-892). Junco et al. is asserted to teach the complexation of the pharmaceutically active substance naproxen with 8-cyclodextrin using super-critical CO_2 (page 69, abstract). Junco et al. is further asserted to teach that the addition of a small amount of co-solvent to a supercritical fluid can have dramatic effects on its solvent power (page 70, left column, lines 4-6. Junco et al. is asserted to teach embodiments wherein the dense pressurized fluid is at a pressure of 125 bar, or 12.5 MPa, at 65 °C (page 70, right column, paragraph 3) or 160 bar, or 16.0 MPa, at 62 °C with stirring (page 70, right column, paragraph 4) and that at the end of the complexation the system is depressurized by venting (page 70, right column, paragraph 4).

The Examiner asserts that Junco et al. does not specifically teach the claimed step "d." of adding to and mixing with the active substance/host molecule molecular complex an agent for interaction with the complex in a semi-solid medium (instant claim 11).

Majid et al. is alleged to teach that it is routine in the field of inclusion complexes of cyclodextrins to perform a step of pelletization or agglomeration after complex formation, from which the invention of Majid et al. forms an improvement (column 2, lines 5-20). Majid et al. is further relied on as teaching that it is advantageous for water to be present during the formation

of the agglomerates (column 2, lines 20-35), thus providing guidance for selecting the mixing performed in a semi-solid medium. Majid et al. is asserted to teach mixing with a Spex mixer in a glass jar sealed tightly (column 3, lines 30-35), implicitly under atmospheric pressure. The Examiner asserts that Majid et al. teaches that any final wet pelletization procedure may be used to form the final agglomerates (column 2, lines 45-55) and that added water has been found necessary for agglomeration (column 2, lines 55-60). The water taught by Majid et al. is interpreted by the Examiner as the agent for interaction with the complex and the Examiner asserts that it is well known that water is an amphoteric substance, in that it can react as an acid or a base.

The Examiner states that it would have been obvious to one of ordinary skill in the art at the time of the invention to combine Junco et al. with Majid et al. because Majid et al. teaches it is routine in the field of inclusion complexes of cyclodextrins to perform a step of pelletization or agglomeration after complex formation.

In response to Applicants' arguments of December 30, 2009, the Examiner asserts that the instant invention as recited by the language in the claims is interpreted as encompassing the method made obvious by Junco et al. in view of Majid et al. in which Junco et al. teaches the complex formation (instant steps a-c) and Majid et al. teaches a step of agglomeration or wet pelletization (instant steps d-e) to give an agglomerated or pelletized form of aqueous soluble inclusion compound.

Applicants traverse this rejection and withdrawal thereof is respectfully requested. The present invention, as encompassed by amended claim 11, drawn to,

> A process for the preparation of an aqueous soluble inclusion compound comprising one or more active substances included in one or more host molecules, the active substance or substances not being very soluble in an aqueous medium, wherein it comprises the following successive steps:
>
> a. bringing one or more active substances into contact with one or more host molecules,
>
> b. carrying out a step of molecular diffusion by bringing a dense pressurized fluid into contact, in static mode, with the mixture obtained in step (a) in the presence of water as a diffusion agent in an amount of between 1 and 50% by weight with respect to the total weight,
>
> c. depressurizing and recovering the active substance/host molecule molecular complex thus formed,

d. carrying out a step which consists of adding to and mixing with the active substance/host molecule molecular complex an agent for interaction with the complex under atmospheric pressure in a semi-solid medium wherein said agent for interaction with the complex is an acid or a base,

e. recovering the aqueous soluble inclusion compound thus formed.

Claim 11 defines the diffusion agent in the recited process as being water, wherein the water is in an amount of between 1 and 50% by weight with respect to the total weight. Neither Junco et al. nor Majid et al. teach or suggest a process for the preparation of an aqueous soluble inclusion compound, wherein water is used as the diffusion agent in the amount recited in claim 11. Applicants note that the Examiner takes the position in the Advisory Action of July 16, 2010, that Junco uses reagent grade methanol in the reference procedure. Thus, the Examiner asserts, Junco has some trace amount of water present. While not acquiescing to the proposition that Junco may have trace amounts of water present, in the interest of facilitating the allowance of the claims, claim 11 has been amended to define the water amount as "between 1 and 50% by weight with respect to the total weight". Thus, the present invention is clearly distinguished from any disclosure in Junco and the instant invention cannot be achieved by the combined teachings of Junco et al. and Majid et al. The claimed invention is therefore not obvious over the reference disclosures and withdrawal of the rejection is respectfully requested.

Claims 11-21 and 26 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Junco et al. in view of Majid et al. and Lieberman et al. (Pharmaceutical dosage forms-- disperse systems, 1998, Marcel Dekker, Inc., 2nd ed., p1-46, cited in PTO-892).

Further to the asserted teachings of Junco et al. and Majid et al. as discussed above, Lieberman et al. is asserted to teach flocculated suspensions made by agglomeration (page 18, paragraph 2-4) and that it is routine in the art to formulate physically stable pharmaceutical suspensions using wetting agents, flocculating agents, stabilizers and preservatives (spanning pages 26-27, section V. FORMULARION OF SUSPENSIONS). Lieberman et al. is further relied upon for teaching stabilizers that include disodium edetate (page 30, paragraph 2), or ethylenediaminetetraacetic acid, a compound that contains both amine and a carboxylic acid moieties, or an amino acid and preservatives that include carboxylic acids such benzoic acid and sorbic acid (page 31, paragraph 1 and page 32, table 9).

The Examiner asserts that it would have been obvious to one of ordinary skill in the art at the time of the invention to combine Junco et al. in view of Majid et al. and Lieberman et al. The Examiner states that the instant method as claimed is interpreted as encompassing making the inclusion complex of cyclodextrin taught by Junco et al. (steps a-c) followed by formulation by pelletization or agglomeration taught by Majid et al. and Lieberman et al. (steps d-e) to prepare an aqueous soluble inclusion compound as part of a pharmaceutical suspension and that one of ordinary skill in the art would have been motivated to combine Junco et al. in view of Majid et al. and Lieberman et al. because Majid et al. teaches it is routine in the prior art in the field of inclusion complexes of cyclodextrins to perform a step of pelletization or agglomeration after complex formation and Lieberman et al. teaches the routine formulation of physically stable pharmaceutical suspensions.

In response to Applicants' arguments of December 30, 2009, the Examiner asserts that with regard to step e., the definition of "recovering" within the chemical arts is interpreted that it is not limited to separation, which is one definition within the chemical arts, but rather the ordinary definition of "recovering" is encompassed and included by the term within the context of the chemical arts. The Examiner states that the term is interpreted to encompass to recovering the aqueous soluble inclusion compound as part of a pharmaceutical formulation from a pelletization or agglomeration mixer because the term "recovering" is not clearly defined to require separating, isolating or purifying said aqueous soluble inclusion compound.

Applicants traverse this rejection and withdrawal thereof is respectfully requested. As discussed above, neither Junco et al. nor Majid et al. teach or suggest a process for the preparation of an aqueous soluble inclusion compound, wherein water is used as the diffusion agent. Lieberman et al. fails to make up for the deficiencies in Junco et al. and Majid et al., since Lieberman et al. similarly fail to teach the use of water as a diffusion agent. In addition, while Lieberman et al. teach obtain a stabilized pharmaceutical suspension, the reference does not teach how to stabilize a complex. As such, the invention of claims 11-21 and 26 is not obvious over Junco et al. combined with Majid et al. and Lieberman et al. and withdrawal of the rejection is respectfully requested.

Claim 27 is further distinguished from the cited references with regard to the feature that the agent for interaction is defined as being chosen from acetic acid, tartaric acid, citric acid, gluconic acid, malic acid, lactic acid, maleic acid, fumaric acid, L-lysine, L-valine, L-isoleucine, L-arginine and aqueous ammonia. None of Junco et al., Majid et al., or Lieberman et al. disclose or suggest an agent for interaction, which is acetic acid, tartaric acid, citric acid, gluconic acid, malic acid, lactic acid, maleic acid, fumaric acid, L-lysine, L-valine, L-isoleucine, L-arginine or aqueous ammonia. As such, claim 27 is further distinguished from not obvious over Junco et al., Majid et al. and/or Lieberman et al.

Should there by an outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact MaryAnne Armstrong, PhD, Registration No. 40069 at the telephone number of the undersigned below to conduct an interview in an effort to expedite prosecution in connection with the present application.

If necessary, the Director is hereby authorized in this, concurrent, and future replies to charge any fees required during the pendency of the above-identified application or credit any overpayment to Deposit Account No. 02-2448.

Dated: JUL 28 2010

Respectfully submitted,

By _____

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